REMARKS

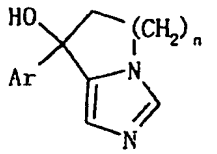
Prior to this amendment, claims 1-34 were pending. Claims 1-34 were rejected. Claims 1-6, 10 and 13-22 have been canceled without prejudice. Claims 7, 8, 9, 11, 12, 23-34 have been amended. New claim 35 has been added. No claims have been cancelled. No new matter has been added by this amendment.

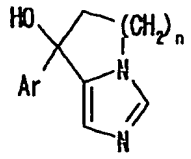
Applicants respectfully reserve the right to pursue any non-elected, canceled or otherwise unclaimed subject matter in one or more continuation, continuation-in-part, or divisional applications.

It is submitted that the claims, herewith and as originally presented were in full compliance with the requirements of 35 U.S.C. § 112. The amendment of the claims, as presented herein, is not made for purposes of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112. Rather, this amendment is made simply for clarification and to round out the scope of protection to which Applicants are entitled. Furthermore, it is explicitly stated that the herewith amendment should not give rise to any estoppel.

Reconsideration and withdrawal of the rejections of this application in view of the amendments and remarks herewith, is respectfully requested, as the application is in condition for allowance.

1. Claims 1-6, 8, 14, 24 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Tasaka et al. (WO 02/40484).

> The Examiner states, "The claimed invention is a controlled release composition for oral administration which comprises a physiologically active substance which is a compound represented by the formula:
>
> 
>
> (I)-A
>
> where n is an integer of 1 to 3, and Ar is an aromatic ring which may be substituted, or a salt thereof, and a hydrophilic polymer. Tasaka teaches a compound of the formula:



(I)

wherein n is an integer of 1 to 3; and Ar is an optionally substituted aromatic ring, or a salt thereof (Page 4, lines 1-8). The compound (+)-6-(7-hydroxy- 6, 7-dihydro- 5H-pyrrolo [1,2-c] imidazol-7-yl)-N-methyl-2-naphthamide is disclosed as one of the compounds (Page 6, lines 24-25). A pharmaceutical composition containing the compound, which is an antitumor agent, and which is an agent for the prophylaxis or treatment of breast cancer or prostate cancer is disclosed (Page 8, lines 6-14). Pharmaceutically acceptable carriers that are used in the composition, including an excipient, a lubricant, a binder, a disintegrating agent and a thickener are disclosed (Page 39, lines 29-33). "Preferable examples of the excipient include lactose, sucrose, D-mannitol, starch, ... Preferable examples of the lubricant include magnesium stearate, calcium stearate, talc, colloidal silica ... Preferable examples of the binder include ... hydroxypropylcellulose, hydroxypropylmethylcellulose ... Preferable examples of the disintegrating agent include starch, carboxymethyl cellulose, carboxymethyl cellulose calcium, crosscarmellose sodium, sodium carboxymethyl starch ... Preferable examples of the thickener include natural gums ... Preferable examples of the solvent include ... propylene glycol ... Preferable examples of the dispersing agent include polyethylene glycol ... Preferable examples of the solubilizer include polyethylene glycol, propylene glycol ... Preferable examples of the isotonicity agent include ... glycerine ..." (Page 40, lines 4-33). The reference also discloses that a tablet, powder, granule or capsule can be prepared by adding "an excipient, a disintegrating agent, a binder, a lubricant and the like to the compound of the present invention, and subjecting the mixture to compression molding, and where necessary, coating for masking of taste, enteric coating or coating for sustention" (Page 41, lines 12-18). The pharmaceutical preparation can be administered orally (Page 42, lines 26-28) and a sustained release preparation can also be administered (Page 43, lines 8-9). Example 5 discloses the production of 6-(7-hydroxy- 6, 7-dihydro- 5H-pyrrolo [1,2-c] imidazol-7-yl)-N-methyl-2-naphthamide (Page 58, line 12 to Page 59, line 8).

Regarding instant claim 1, the controlled release composition is anticipated by the composition comprising the compound of formula (I) and the sustained release preparation disclosed by Tasaka (Page 4, lines 1-8 and Page 43, lines 8-9).

The limitation of the hydrophilic polymer is anticipated by the hydroxypropylcellulose and hydroxypropylmethylcellulose taught by Tasaka (Page 40, lines 8-10).

Regarding instant claim 2, the limitation of a core that is coated with a coating layer containing a polymer is anticipated by the "enteric coating or coating for sustention" on the tablets taught by Tasaka (Page 41, lines 12-18). A coating layer will inherently coat a core of material. An enteric coating will inherently have an enteric coating polymer or enteric coating material.

Regarding instant claims 3 and 24, the solubility of the physiologically active substance is anticipated by the compound of formula (I) disclosed by Tasaka (Page 4, lines 1-8). The solubility of a compound is an inherent property of the compound and since the compound of formula (I) is taught by Tasaka, the solubility of the compound is anticipated by Tasaka.

Regarding instant claims 4 and 6, the dissolution characteristics of the controlled release composition is anticipated by the composition comprising the compound of formula (I) and the sustained release preparation disclosed by Tasaka (Page 4, lines 1-8 and Page 43, lines 8-9). The dissolution characteristics of a composition are an inherent property of the composition and since a composition comprising the compound of formula (I) is taught by Tasaka, the dissolution characteristics of the composition is anticipated by Tasaka.

Regarding instant claim 5, the controlled release composition is anticipated by the composition comprising the compound of formula (I) disclosed by Tasaka (Page 4, lines 1-8 and Page 43, lines 8-9). The hydrophilic polymer is anticipated by the hydroxypropylcellulose and hydroxypropylmethylcellulose taught by Tasaka (Page 40, lines 8-10). The lubricant is anticipated by the magnesium stearate, calcium stearate, talc and colloidal silica taught by Tasaka (Page 40, lines 6-8).

Regarding instant claim 8, the rapid release property of the physiologically active substance in the absence of the coating layer is anticipated by the tablet without a coating layer as disclosed in Preparation Example 2 by Tasaka (Page 76, lines 12-23). A tablet without a coating layer will inherently have the property of rapid release of the active substance when compared to a tablet with a coating layer.

Regarding instant claims 14 and 27, the use of the controlled release composition for treating prostate cancer or breast cancer is anticipated by the pharmaceutical composition used for the treatment of breast cancer or prostate cancer as taught by Tasaka (Page 8, lines 6-14). Moreover, the use of the controlled release

composition for "prevention" of prostate cancer or breast cancer is an intended use and has no significance in composition claims.

Therefore, the limitations of claims are anticipated by the teachings of Tasaka.".

Claims 1 – 6 have been canceled without prejudice and, consequently, the basis for the rejections have been obviated. Claims 8, 14, 24 and 27 have been amended to be dependent from amended claim 7 and are now longer dependent from canceled claim 2, and thus, similarly the basis for rejection of these claims has been obviated.

2. Claims 7, 9-12, 22-23 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tasaka et al. (WO 02/40484) in view of Okada et al. (US 5,807,880).

The Examiner states, "The teaching of Tasaka is stated above.

Tasaka does not expressly teach enteric coating agents.

Okada teaches a steroid 17-20 lyase inhibitor, a pharmaceutically acceptable salt and a pharmaceutical composition (Col. 1, lines 6-8). The solid composition for oral administration may be used in the dosage form of tablets, powders or granules. "The tablets or pills may be coated with a gastric or enteric film such as of sucrose, gelatin, hydroxypropylcellulose, hydroxypropylmethylcellulose phthalate or the like" (Col. 10, lines 10-14).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition comprising the compound of formula (I) and an enteric coating, as suggested by Tasaka, combine it with the composition comprising a steroid 17-20 lyase inhibitor that may be coated with a gastric or enteric film such as hydroxypropylmethylcellulose phthalate, as suggested by Okada, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Tasaka teaches that the composition can have an enteric coating and Okada teaches the specific enteric coating agents for solid compositions of a steroid 17-20 lyase inhibitor. One with ordinary skill in the art would use enteric coatings to ensure the protection of the composition through the gastric passage and to further ensure the release of the active ingredient in the intestines.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Regarding instant claim 7, the controlled release composition is taught by the composition comprising the compound of formula (I) disclosed by Tasaka (Page 4, lines 1-8 and Page 43, lines 8-9). The hydrophilic polymer is taught by the hydroxypropylcellulose and hydroxypropylmethylcellulose by Tasaka (Page 40, lines 8-10). The lubricant is taught by the magnesium stearate, calcium stearate, talc and colloidal silica by Tasaka (Page 40, lines 6-8). The enteric coating would have been obvious over the enteric coating of the composition taught by Tasaka (Page 41, lines 12-18) in view of the hydroxypropylmethylcellulose phthalate used as an enteric coating agent, as taught by Okada (Col. 10, lines 10-14).

Regarding instant claim 9, the limitation of the core as a controlled release matrix which further comprises a hydrophilic polymer would have been obvious over the hydrophilic polymers (hydroxypropylcellulose and hydroxypropylmethylcellulose) taught by Tasaka (Page 40, lines 8-10).

Regarding instant claims 10 and 25, the limitation of the hydrophilic polymer used at about 3% to about 95% by weight would have been obvious over the hydrophilic polymers (hydroxypropylcellulose and hydroxypropylmethylcellulose) taught by Tasaka (Page 40, lines 8-10) and by the 3% of hydroxypropylcellulose (calculated 10% of 210g=21g, 21g/700g tablet core=3%) used in the tablet composition disclosed by Okada (Col. 19, lines 46-58).

Regarding instant claims 11-12, the pH dependent or delayed-dissolution type water solubility of the polymer in the coating layer and the insoluble or sparingly soluble polymer in the coating layer would have been obvious over the enteric coating of the composition taught by Tasaka (Page 41, lines 12-18) in view of the hydroxypropylmethylcellulose phthalate used as an enteric coating agent, as taught by Okada (Col. 10, lines 10-14). One with ordinary skill in the art would know that enteric coating polymers are water insoluble, pH dependent, and delay the dissolution of the active ingredient until after the acidic pH of the gastric passage.

Regarding instant claims 22-23, the compound would have been obvious over the (+)-6-(7-hydroxy- 6, 7-dihydro- 5H-pyrrolo [1,2-c] imidazol-7-yl)-N-methyl-2-naphthamide taught by Tasaka (Page 6, lines 24-25). The disintegrant would have been obvious over the disintegrating agents taught by Tasaka (Page 40, lines 11-14). The lubricant would have been obvious over the magnesium stearate, calcium stearate, talc, colloidal silica taught by Tasaka (Page 40, lines 6-8). The enteric coating agent would have been obvious over the hydroxypropylmethylcellulose phthalate taught by Okada (Col. 10, lines 10-14). The binder would have been obvious over the lactose, sucrose, D-mannitol, starch taught by Tasaka (Page 40, lines 4-5). The plasticizer would have been obvious over the glycerin, polyethylene glycol and propylene glycol taught by Tasaka (Page 40, lines 33 and 22).".

The PTO has issued Examination Guidelines for Determining Obviousness Under 35 U.S.C. § 103 ("Guidelines") in view of the Supreme Court's recent decision in KSR International Co. v. Teleflex Inc., 550 U.S. __, 82 USPQ2d 1385 (2007), The Guidelines were published in the Fed. Reg., Vol. 72, no. 195, October 10, 2007. As pointed out in the Guidelines, the Supreme Court in KSR reaffirmed the analytical framework for determining obviousness as set forth in Graham v. John Deere Co., 338 U.S. 1, 148 USPQ 459 (1966), and also held that the Federal Circuit's application of its teaching-suggestion-motivation test was too formalistic.

Under Graham, obviousness is a question of law based on underlying factual inquiries that address (1) the scope and content of the prior art, (2) the differences between the claimed invention, and (3) resolving the level of ordinary skill in the pertinent art. Consideration must also be given to secondary factors, such as, for example, evidence of commercial success, long felt but unsolved needs, failure of others, and unexpected results. The Supreme Court stated in KSR that "While the sequence of these questions might be reordered in any particular case, the [Graham] factors continue to define the inquiry that controls." The Guidelines go on to state that "Once the *Graham* factual inquiries are resolved, Office personnel must determine whether the claimed invention would have been obvious to one or ordinary skill in the art."

The Guidelines proceed then to articulate seven independent rationales on which to properly base a rejection under 35 U.S.C. § 103: (1) combining prior art elements according to known methods to yield **predictable results**, (2) substitution of one known element for another to obtain **predictable results**, (3) use of known technique to improve similar devices, methods or products in the same way, i.e., to obtain **predictable results**, (4) applying a known technique to a known device, method or product ready for improvement to yield **predictable results**, (5) choosing from a finite number of identified, **predictable solutions**, with a reasonable expectation of success, i.e., obvious to try, (6) evidence of design incentives or other market forces sufficient to prompt skilled artisan to vary prior art in a **predictable manner** to result in claimed invention, and (7) evidence of some teaching, suggestion, or motivation in the prior art

that would have led the skilled artisan to modify or combine prior art to arrive at claimed invention, i.e., **predictable** modification. All of these tests have the requirement of **predictability**. That is lacking in the present case.

Given the amendments to claim 7, Applicants respectfully disagree. The enteric coating of claim 7 has now been limited to methacrylic acid copolymers which is not taught or suggested by the Tasaka or Okada references. Applicants respectfully request reconsideration.

3. Claims 13, 15-21, 26 and 28-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tasaka et al. (WO 02/40484) in view of Fernandez et al. (US 3,696,188).

> The Examiner states, "The teaching of Tasaka is stated above.
>
> Tasaka does not expressly teach a coating layer which contains a physiologically active substance.
>
> Fernandez teaches a laminated, pan-coated tablet comprising a medicament-containing or inert compressed tablet core surrounded by a plurality of pan-coated medicament-containing subcoating layers comprised of active ingredients (Col. 3, lines 5-9).
>
> It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition comprising the compound of formula (I) and an enteric coating, as suggested by Tasaka, combine it with the coating containing active ingredients, as suggested by Fernandez, and produce the instant invention.
>
> One of ordinary skill in the art would have been motivated to do this because Fernandez teaches that laminated tablets with a medicament in a layer surrounding the core are "useful for various purposes, such as achieving differential release in rate ..." (Col. 1, lines 14-15).
>
> Regarding instant claim 13, the coating layer which contains a physiologically active substance would have been obvious over the coating of the composition taught by Tasaka (Page 41, lines 12-18) in view of the coating containing active ingredients, as taught by Fernandez (Col. 3, lines 5-9).
>
> Regarding instant claims 15-20 and 26, the composition combined with at least one other controlled release composition

would have been obvious over the composition comprising the compound of formula (I) as taught by Tasaka (Page 4, lines 1-8 and Page 43, lines 8-9) in view of the medicament-containing subcoating layers taught by Fernandez (Col. 3, lines 5-9). One with ordinary skill in the art would use the compound of formula (I) as the medicament in the coating layer during the process of routine experimentation in order to optimize the release profile of the active ingredient.

Regarding instant claims 21 and 34, the use of the controlled release composition for treating prostate cancer or breast cancer is taught by the pharmaceutical composition used for the treatment of breast cancer or prostate cancer as taught by Tasaka (Page 8, lines 6-14). Moreover, the use of the controlled release composition for "prevention" of prostate cancer or breast cancer is an intended use and has no significance in composition claims.

Regarding instant claims 28-33, the limitation of a different release rate of a physiologically active substance would have been obvious over the composition with the compound taught by Tasaka (Page 4, lines 1-8 and Page 43, lines 8-9) in view of the differential release rates in the coated compositions taught by Fernandez (Col. 1, lines 14-15).".

Applicants respectfully disagree. Applicants reiterate the "Guidelines" recited above. With regard to claims 13 and 15-21, these claims have been canceled without prejudice, and therefore, the basis for these claim rejections has been obviated. Furthermore, with regard to claims 26 and 28-34, these claims are all dependent from amended claim 7 which relates to "a coating layer". The Examiner states in the basis for rejection, "Fernandez teaches a laminated, pan-coated tablet comprising a medicament-containing or inert compressed **tablet core surrounded by a plurality of pan-coated medicament-containing subcoating layers** comprised of active ingredients (Col. 3, lines 5-9). The present invention relates to a single coating, not a plurality of coating layers. Therefore, it would not be obvious to one of ordinary skill in the art in view of Tasaka and Fernandez to achieve the present invention. Applicants respectfully request reconsideration.

CONCLUSION

In view of the remarks made herein, the application is believed to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are respectfully requested. Please charge any required fee or credit any overpayment to Deposit Account No. 04-1105.

Dated: May 29, 2008

Respectfully submitted,

By _____

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